Title **WO9918206A2: NOVEL HUMAN CANCER ANTIGEN NY ESO-1/CAG-3 AND GENE ENCODING SAME**

Country: **WO** World Intellectual Property Organization (WIPO)

Kind: **A2** Publ.of the Int.Appl. without Int.search REP.

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No Image

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Issued/Filed Dates: **April 15, 1999** / Sept. 21, 1998

Application Number: **WO1998US0019609**

IPC Class: **C12N 15/12;** C07K 14/47; A61K 38/08; A61K 38/10; A61K 38/17; C12N 15/11; C12N 15/86; C07K 16/18; C12Q 1/68; A61K 35/14; A01K 67/027; C12N 5/08;

ECLA Code: **C07K14/47A34;**

Priority Number(s): Oct. 8, 1997 **US1997060061428**

INPADOC Legal Status: Show legal status actions

Designated Countries: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, **European patent:** AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, **OAPI patent:** BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG, **ARIPO patent:** GH, GM, KE, LS, MW, SD, SZ, UG, ZW, **Eurasian patent:** AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

Abstract: The present invention discloses the identification, isolation and cloning of a gene encoding a novel cancer antigen NY ESO-1/CAG-3 and peptides thereof derived from various open reading frames from the NY ESO-1 gene. The novel cancer antigen and peptides are recognized by cytotoxic T lymphocytes in an HLA restricted manner. The products of the gene are promising candidates for

immunotherapeutic strategies for the prevention, treatment and diagnosis of patients with cancer.
[Show in French]

Attorney, Agent, or Firm: **FEILER, William, S. ;**

Related Applications:

Application	ApplDate	Patent	Issued	Title
US1997060061428	1997-10-			

Family: Show known family members

Description: Expand full description

+ **NOVEL HUMAN CANCER ANTIGENNY**
+ **FIELD OF THE INVENTION**
+ **BACKGROUND OF THE INVENTION**
+ **SUMMARY OF THE INVENTION**
+ **BRIEF DESCRIPTION OF THE FIGURES**
+ **DETAILED DESCRIPTION OF THE INVENTION**

Claims:
[Hide claims]:

I A cancer peptide, functional portion or derivatives thereofencoded within a nucleic acid sequence of SEQ. ID NO: I and variants thereof.

2.A cancer peptide, function portion or derivative according toclaim I wherein the peptide is encoded by SEQ. ID NO: 2 or portion thereof.

3.A cancer peptide, functional portion or derivative according toclaim I wherein the peptide is encoded by SEQ. ID NO: 3 or portion thereof

4.A cancer peptide comprising SEQ. ID NO: 4 or portion orderivative thereof1 0 5. A cancer peptide comprising SEQ. ID NO: 5 or portion orderivative thereof

6.A cancer peptide, portion or derivative thereof according toclaim 1-4 or 5 wherein the cancer peptide is immunologically recognized by HLArestricted T lymphocytes.1 5 7. A cancer peptide, portion or derivative thereof according toclaim 1-4 or 5 wherein the T lymphocytes are MHC class I restricted.

8.A cancer peptide, portion or derivative thereof according toclaim 1-6 or 7 wherein the cancer peptide is derived ftom a cancer selected from thegroup consisting of. a non-Hodgkins lymphoma, leukemia, Hodgkins lymphoma, lung2 0 cancer, liver cancer, metastases, melanoma, adenocarcinoma, thymoma, colon cancer,uterine cancer, breast cancer, prostate cancer, ovarian cancer, cervical cancer, bladdercancer, kidney cancer, pancreatic cancer and sarcoma.

9.A cancer peptide, portion or derivative thereof according toclaim 1-7 or 8 wherein the cancer peptide or portion thereof is present on primary2 5 breast tumor isolates and melanoma cells.

10.A cancer peptide, portion or derivative thereof according toclaim I wherein the peptide is encoded by a nucleic acid sequence comprising SEQ.ID NO: 5 1.-

11.A cancer peptide, portion or derivative thereof according toclaim 1 or 2 wherein the cancer peptide comprises at least the amino acid sequence:ASGPGGGAPR (SEQ ID NO.: 25), or derivative thereof.

12.A cancer peptide according to claim 1 1, further comprising anaddition of I to about 10 amino acids at the N-tenninus of SEQ. ID

NO: 25.

13.A cancer peptide according to claim 1 1, further comprising anaddition of I to about 5 amino acids at the N-terminus of SEQ. ID NO: 25.

14.The cancer peptide, portion or derivative thereof according toclaim 1 or 2 wherein the cancer peptide comprises the amino acid sequence:0 ASGPGGGAPK (SEQ. ID NO: 39).

15.The cancer peptide, portion or derivative thereof according toclaim 1 or 2 wherein the cancer peptide comprises the amino acid sequence:AGAARASGPGGGAPR (SEQ. ID NO: 26)

16.The cancer peptide, portion or derivative thereof according to5 claim I or 2 wherein the cancer peptide comprises the amino acid sequence:RGPRGAGAARASGPGGGAPR (SEQ. ID NO: 45).

17.A cancer peptide, portion or derivative thereof according toclaim I or 2 wherein the cancer peptide comprises the amino acid sequence:TVSGNILTIR (SEQ. ID NO: 15).0 1 S. A cancer peptide or analog thereof comprising the amino acidsequence:Xaa, Xaa2 Xaa3GPGGGAPXaa, (SEQ. ID NO: 54)wherein Xaa, is no amino acid or one to IO amino acids, Xaa2 is Ala,Thr, Val, Leu or Arg, Xaa3 is Ser or a conservative amino acid substitution, and Xaa, isArg or Lys.

19.The cancer peptide according to claim 18 wherein theconservative amino acid at Xaa, is selected from the group consisting of Ala, Val, Ile,Leu and Thr.- 65 -

20.The cancer peptide according to claim 18 wherein Xaa, is atleast one amino acid selected from the group consisting of Ala, Gly, Arg orcombinations thereof

21.The cancer peptide according to claim 18 wherein Xaa, is Ala,Val or Thr.

22.The cancer peptide according to claim 18 wherein Xaa2 is Arg-

23.The cancer peptide according to claim 18 wherein Xaa, is Argand Xaa, is one to 5 amino acids selected from the group consisting of Ala, Gly, Argor combinations thereof1 0 24. A cancer peptide, portion or derivative thereof encoded by analternative open reading frarne of SEQ. ID NO: 3, variant or homolog thereof.

25.A cancer peptide, portion or derivative thereof according toclaim 24 wherein the peptide has SEQ. ID NO: 27.

26.A cancer peptide, portion or derivative thereof according to1 5 claim 24 wherein the peptide comprises the amino acid sequence:LAAQERRVPR (SEQ. ID NO: 47).

27.A cancer peptide, portion or derivative thereof according toclaim 24 wherein the peptide comprises the amino acid sequence:AAQERRVPR (SEQ. ID NO: 46).2 0 28. A pharmaceutical composition comprising at least one cancerpeptide according to claims 1-26 or 27 and a pharmaceutically acceptable carrier.

29.A pharmaceutical composition consisting essentially of SEQ. IDNO. 4, SEQ. ID NO: 5, SEQ. ID NO: 14, SEQ. ID NO: 25, SEQ. ID NOS: 34-38,41,

42.46, 47 or combinations thereof and a phannaceutically acceptable carrier.

30.A immunogen comprising the cancer peptide according toclaims 1-26 or 27 alone or in combination with at least one immunostimulatorymolecule.

31.A immunogen according to claim 30 wherein the- 66 - immunostimulatory molecule is an HLA molecule.

32.An isolated nucleic acid sequence comprising SEQ ID NO: 1,portion or homolog thereof

33.An isolated nucleic acid sequence according to claim 32wherein the nucleic acid sequence comprises SEQ ID NO.: 2 or 3

or portion or variantthereof.

34.An isolated nucleic acid sequence according to claim 32wherein the nucleic acid sequence encodes an alternative open reading frame geneproduct.1 0 35. An isolated nucleic acid sequence according to claim 32wherein the sequence encodes an amino acid sequence:ASGPGGGAPR (SEQ ID NO.: 25), or derivative thereof

36.An isolated nucleic acid sequence encoding the ORF2 peptideof SEQ. ID NO: 5.1 5 37. An isolated nucleic acid sequence according to claim 36wherein the nucleic acid sequence encodes a cancer peptide having the amino acidsequence:LAAQERRVPR (SEQ. ID NO: 47).

38.An isolated nucleic acid sequence according to claim 36wherein the nucleic acid sequence encodes a cancer peptide having the amino acidsequence:AAQERRVPR (SEQ. ID NO: 46).

39.A recombinant expression vector comprising the nucleic acidsequence according to claims 32-37 or 38.

40.A host organism transformed or transfected with a recombinantexpression vector according to claim 39.

41.A host organism according to claim 40 wherein the hostorganism is an antigen presenting cell.- 67 -

42.An oligonucleotide comprising a nucleic acid sequencecomplementary to the nucleic acid sequence according to claims 32-37 or 38.

43.A recombinant virus comprising a recombinant virus which hasincorporated into a viral genome or portion thereof the nucleic acid sequenceaccording to claims 32-37 or 38.

44.A recombinant virus according to claim 43 further comprising atleast one gene encoding an immunostimulatory molecule.

45.The recombinant virus according to claim 43 wherein the virusis selected from the group consisting of retrovirus, baculovirus, Ankara virus, fowlpox,1 0 adenovirus, and vaccinia virus.

46.The recombinant virus according to claim 43 wherein the cancerpeptide is derived from melanocytes.

47.A recombinant virus according to claim 44 wherein theinummostimulatory molecule is a HLA class I molecule.1 5 48. A host organism transformed or transfected with therecombinant virus according to claim 43-46 or 47.

49.An isolated antibody or antigen binding portion thereof thatbinds the cancer peptide, or portion thereof encoded by SEQ. ID NO: 1, SEQ. ID NO:2 or SEQ. ID NO: 3.2 0 50. An isolated antibody that binds the cancer peptide or antigenicportion thereof of SEQ. ID NO: 4 or SEQ. ID NO: 5.

51.An isolated antibody that binds a cancer antigen encoded bySEQ ID NOS: 4, 5, 6, 14, 25, 34-38, 41, 42, 46, 47 or a fragment thereof.

52.An isolated antibody that binds the cancer peptide, antigen or2 5 variant thereof of claim 1 1.

53.A method of producing a recombinant cancer peptide or portionthereof comprising:a. inserting a nucleotide sequence of SEQ ID NO.: 1, 2 or 3-or portion or variant thereof, into an expression vector;b. transferring the expression vector into a host cell;C. culturing the host cell under conditions appropriate forexpression of the cancer peptide or portion thereof, andd. harvesting the recombinant cancer peptide, or portionthereof

54.A method according to claim 53 further comprising in step (a) inserting a nucleotide sequence encoding an HLA class I molecule, or portion thereofinto the expression vector.1 0 55. A method of detecting the presence of cancer or precancer in amammal comprising:a. contacting a nucleic acid sequence of SEQ ID NO.: 1, 2or 3 or portion or variant thereof with a test biologicalsample of

mRNA taken from the mammal under1 5 conditions allowing for a complex to form between thesequence and the mRNA;b. detecting the complex;C. comparing the amount of niRNA in the test sample withan amount of mRNA from a known normal biological2 0 sample, wherein an increased amount of mRNA fromthe test sample is indicative of cancer or precancer.

56.A method according to claim 55 wherein the cancer orprecancer is melanoma.

57.A method according to claim 55 wherein the biological sample2 5 is from breast tissue.

58.A method of detecting an CAG-3 genomic nucleic acidsequence in a biological sample comprising:a. contacting the genomic nucleic acid sequence with SEQ- 69 -ID NO.: 1, 2 or 3 or portion or variant thereof underconditions to allow complexes to form between thegenomic nucleic acid sequence; andb. detecting the complex.

59.A method of detecting the cancer peptide or portion thereofaccording to claims 1-26 or 27 in a biological sample comprising:a. contacting the sample with antibodies specific for saidcancer peptide under conditions to form an immunecomplex, and1 0 b. detecting the presence of the immune complex.

60.A method of preventing or inhibiting cancer in a mammalcomprising: administering to the mammal an effective amount of the cancer peptide,or portion thereof according to claims 1-26 or 27, alone or in combination with anHLA molecule, said amount is effective in preventing or inhibiting the cancer in the1 5 mammal.

61.A method of inhibiting melanoma in a mammal comprising:a. exposing T lymphocytes in vitro to a cancer peptide,tumor antigen or portion thereof according to claims 1 -26 or 27, alone or in combination with an MHC2 0 molecule for a time sufficient to elicit cancer peptidespecific T lymphocytes;b. administering the cancer peptide specific T lymphocytesto the mammal in an amount sufficient to inhibit themelanoma.2 5 62. A method of preventing or inhibiting cancer in a mammalcomprising: administering to the mammal an effective amount of the cancer peptideaccording to claims 1-26 or 27 alone, or in combination with an HLA molecule, saidamount is effective in preventing or inhibiting cancer in a mammal.- 70 -

63.A method of preventing or inhibiting cancer in a mammalcomprising administering to the mammal an effective amount of a recombinant virusaccording to claims 43-46 or 47 alone or in combination with an exogenousimmunostimulatory molecule said amount is effective in preventing or inhibiting thecancer.

64.A method according to claim 63 wherein the mammal expressesan HLA Class I molecule selected from the group consisting of HLA-A3 1, HLA-A3,HLA-Al I. HLA-A33, or HLA-A68.

65.A pharmaceutical composition comprising the recombinant1 0 virus according to claims 43-46 or 47 alone or in combination with an exogenousimmunostimulatory molecule, chemotherapy drug, antibiotic, antifungal drug, antiviraldrug or combination thereof and a pharmaceutically acceptable carrier.

66.A transgenic animal carrying and expressing a gene encoding acancer antigen comprising at least a fragment of SEQ ID NO: 1.1 5 67. A cancer antigen specific human cytotoxic T lymphocyteelicited by the cancer peptide according to claim 1-26 or 27.

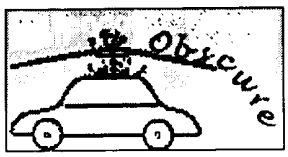
68.The cancer antigen specific human cytotoxic T lymphocyteaccording to claim 67, wherein the lymphocyte recognizes an HLA-A31 molecule.

69.The cancer antigen specific human cytotoxic T lymphocyte2 0 according to claim 67; wherein the lymphocyte recognizes an HLA

Class I moleculeselected from the group consistingof HLA-A3, HLA-Al 1, HLA-A33, and HLA-A68.

Other Abstract Info: CHEMABS 130(21)280849M CHEMABS 130(21)280849M DERABS C1999-277270 DERABS C1999-277270

Foreign References: No patents reference this one



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INPADOC Record

Title: **WO9918206A3: HUMAN CANCER ANTIGEN NY ESO-1/CAG-3 AND GENE ENCODING SAME**

Country: **WO** World Intellectual Property Organization (WIPO)

Kind: **A3** Subsequent Publ. of the Int. search report

Inventor(s): **WANG, RONG, FU**, United States of America
ROSENBERG, STEVEN, A., United States of America

No Image

Applicant/Assignee: **ROSENBERG, STEVEN, A.**, United States of America
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Issued/Filed Dates: **Aug. 5, 1999** / Sept. 21, 1998

Application Number: **WO1998WO0019609**

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ECLA Code: **C07K14/47A34;**

Priority Number(s): Oct. 8, 1997 **US1997000061428**

INPADOC Legal Status:

Gazette date	Code	Description (remarks) List all possible codes for WO
Aug. 10, 2000	**REG**	Reference to national code (DE8642)
April 8, 2000	**NENP**	Non-entry into the national phase in:
Aug. 12, 1999	**DFPE**	Request for preliminary examination filed prior to expiration of 19th month from priority date
Aug. 5, 1999	**AK**	Designated states (AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW)
		Designated countries for regional patents (GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY

Aug. 5, 1999	**AL**	DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG)
Aug. 5, 1999	**A3**	Subsequent publication of the international search report
June 16, 1999	**121**	Ep: pct app. art. 158 (1)
April 15, 1999	**A2**	Publication of the international application without the international search report
April 15, 1999	**AK**	Designated states (AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW)
April 15, 1999	**AL**	Designated countries for regional patents (GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN GW ML MR NE SN TD TG)
Sept. 21, 1998	**AE**	International application
Oct. 8, 1997	**AA**	Priority claimed

Designated Countries: AL, AM, AT, AU, AZ, BA, BB, BE, BF, BG, BJ, BR, BY, CA, CF, CG, CH, CI, CM, CN, CU, CY, CZ, DE, DK, EE, ES, FI, FR, GA, GB, GE, GH, GM, GN, GR, GW, HR, HU, ID, IE, IL, IS, IT, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MC, MD, MG, MK, ML, MN, MW, MX, NE, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, SN, SZ, TD, TG, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

Abstract: The present invention discloses the identification, isolation and cloning of a gene encoding a novel cancer antigen NY ESO-1/CAG-3 and peptides thereof derived from various open reading frames from the NY ESO-1 gene. The novel cancer antigen and peptides are recognized by cytotoxic T lymphocytes in an HLA restricted manner. The products of the gene are promising candidates for immunotherapeutic strategies for the prevention, treatment and diagnosis of patients with cancer.

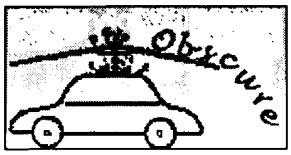
Family:

Patent	Issued	Filed	Title
WO9918206A3	Aug. 5, 1999	Sept. 21, 1998	HUMAN CANCER ANTIGEN NY ESO-1/CAG-3 AND GENE ENCODING SAME
WO9918206A2	April 15, 1999	Sept. 21, 1998	NOVEL HUMAN CANCER ANTIGEN NY ESO-1/CAG-3 AND GENE ENCODING SAME
EP1021535A2	July 26, 2000	Sept. 21, 1998	HUMAN CANCER ANTIGEN NY ESO-1/CAG-3 AND GENE ENCODING

			SAME
AU9572098A1	April 27, 1999	Sept. 21, 1998	NOVEL HUMAN CANCER ANTIGEN NY ESO-1/CAG-3 AND GENE ENCODING SAME
4 family members shown above			

Other Abstract Info: CHEMABS 130(21)280849M DERABS C1999-277270

Foreign References: No patents reference this one



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